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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,968	03/07/2001	Nobuyuki Itoh	PP-17150.001 / 201130.409	8729

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EXAMINER	
SAOUD, CHRISTINE J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/801,968	ITOH et al.
Examiner	**Art Unit**
Christine Saoud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 3, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above, claim(s) *1-11, 19-21, and 23-60* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *12-18, 22, and 61-65* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 16
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 12-18 have been amended and claims 61-65 have been added as requested in the amendment of paper #19, filed 03 June 2003. Claims 1-65 are pending in the instant application. Claims 1-11, 19-21, 23-60 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14. Claims 12-18, 22 and 61-65 are under examination in the instant application.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed 03 June 2003 have been fully considered but they are not deemed to be persuasive.

Drawings

5. Applicant indicates at page 7 of the response (item 3) that the Brief Description of the Drawings has been amended as requested. However, the Brief Description still does not comply

with 37 CFR 1.84(U)(1). The specification must refer to Figure 2A-2B, not just "Figure 2". The specification must refer to Figure 3A-3B, not just "Figure 3". Likewise, the Drawings contain Figures 7A-7B, 8A-8B, 9A-9B, 13A-13B, 15A-15B and the Brief Description of the Drawings should be amended to reflect these Figures. Correction is still required.

Claim Objections

6. Claim 16 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 16 depends from claim 15. Claim 15 requires at least 14 contiguous amino acids, but claim 16 comprises between 10 and 50 contiguous amino acids. Therefore, claim 16 is broader than claim 15 and does not further limit.

7. Claim 18 is objected to because of the following informalities: it has extra words in the claim which appear to be the result of a typographical error. The claim recites "wherein the epitope-bearing portion comprises the epitope-bearing portion comprises amino acids". The additional phrase "the epitope-bearing portion comprises" should be deleted. Appropriate correction is required.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 15-18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 15-18 are directed to "an amino acid sequence", however, this is subject matter which is patentable. An amino acid sequence is merely a representation of a protein molecule on paper, and not the actual protein molecule itself, which is patentable material. This rejection could be avoided by claiming "an isolated polypeptide, comprising at least 14 contiguous amino acids of SEQ ID NO:4" or something to that general effect. The recitation of "epitope-bearing portion" does not appear to be necessary, since the art recognizes that a protein of 5-6 amino acids is sufficient for generation of an antibody, and therefore, anything greater than that in size would be considered an "epitope-bearing portion". The further dependent claims could be then "the isolated polypeptide of claim 15".

Claims 15-18 additionally fail to include any limitations which would distinguish the implied claimed proteins from those which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, mere purity of a naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui, 156 USPQ 426 (1966). However, when purity results in a new utility, patentability is considered. Merck Co. v. Chase Chemical Co., 273 F. Supp. 68 (1967). Filing of evidence of a new utility imparted by the

increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims. The claims are directed to an epitope-bearing portion of a polypeptide, however, the entire protein can be considered an epitope-bearing portion. Furthermore, since the dependent claims include open language of "comprising", this fails to limit the polypeptides to any particular fragment or portion, thereby encompassing the protein as it occurs in nature.

Applicant asserts that the claims have been amended "to clarify that he claimed epitope-bearing region is comprised by an amino acid sequence". However, this still does not remedy the deficiency of the claims, which is that the claims presently encompass naturally occurring protein molecules because there is no indication of the "hand of man" and the language of "comprising" encompasses the full-length, naturally occurring protein.

10. Claims 12-18, 22 and 61-65 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for the reasons of record in paper #15 as applied to claims 12-18 and 22.

Applicant asserts that the claimed invention has a specific utility (see pages 8-9 of the response).

> ... the FGF-23 of the invention is cleaved during expression, resulting in production of a 20 kDa protein and a 7-12 kDa protein (page 7, lines 22-25). "The cleavage may play a role in disorders of phosphate metabolism," (page 7,

lines 28-29). The specification discloses that an FGF-23 that has been mutated to alter or delete the cleavage site provides a composition for treating disorders of phosphate metabolism, wherein the disorder is a result of cleavage of FGF-23 (page 8, lines 1-4). Such mutation is unique to FGF-23, according to a publication cited at page 7, lines 28-29 of the specification.

11. Therefore, the specification speculates that the claimed invention could be used to treat phosphate metabolism disorders which are the result of cleavage of FGF-23, but no such conditions are described in the instant specification. Additionally, the specification speculates that a non-cleavable form of the protein could be used to treat phosphate disorders, but fails to indicate which type of phosphate disorders are to be treated. In other words, will the claimed invention be used to increase phosphate or to decrease phosphate in the body. The role of the claimed invention in phosphate metabolism is not taught nor is there any disclosure of what types of conditions or disorders are to be treated by the administration of the claimed invention or a mutated form of the invention. Therefore the instant specification does not provide a substantial utility for the claimed invention at the time it was filed; ie. a utility that is in currently available form at the time the invention was filed.

The Declaration under 37 CFR 1.132 filed 03 June 2003 is insufficient to overcome the rejection of claims 12-18 and 22 based upon lack of utility as set forth in the last Office action because: the evidence provided therein does not support an assertion of a substantial utility in the instant specification as filed. The Declaration provides evidence that administration of a non-cleavable FGF-23 lowers serum phosphate levels in mice. However, the instant specification does

not disclose use of the claimed invention for lowering serum phosphate levels nor does it indicate which diseases the claimed invention could be used for treating. Therefore, although the asserted utility in the specification was credible and specific, it was not substantial because further research was necessary to confirm a specific and substantial utility for the claimed invention. As the application was originally filed, the skilled artisan did not know what type of disease could be treated by administration of the claimed invention because the role in phosphate metabolism was not established, and therefore, use in the treatment of disease of phosphate metabolism was not a substantial utility (i.e. where specific benefit exists in currently available form).

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 12-18 and 22 are rejected under 35 U.S.C. §112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. §101.

14. Claims 12-13 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues that the specification "discloses growth factors having the biological activity of FGF-23, and a specified degree of homology" (see response at bottom of page 11).

This argument is persuasive because the instant specification fails to disclose the biological activity of FGF-23 (see utility rejection). Additionally, the recitation of %identity fails to indicate which portions of structure are necessary (required) for the biological activity. As the instant specification fails to teach a biological activity possessed by the claimed protein, and therefore, fails to teach an assay for determining whether a variant has the required biological activity, the instant specification fails to describe polypeptides which meet these limitations of these claims. There is a lack of guidance or teaching regarding structure and function of the polypeptide because there are only two examples provided in the specification and because there is no guidance found in the prior art for this specific polypeptide, including a lack of disclosure of activity for the polypeptide. The specification fails to provide a representative number of species for the claimed genus because the specification only teaches two embodiments. Therefore, the claims are directed subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 12-13, 61-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12 and 13 recite "wherein said polypeptide retains the biological activity of human FGF-23". However, the instant specification fails to teach the biological activity of human FGF-23, therefore, one of ordinary skill in the art would not know if such activity is retained. The metes and bounds of what is claimed cannot be determined, and therefore, the claims are indefinite. Claims 61-65 depend from claim 12, and are therefore, also indefinite.

17. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 13 recites the broad recitation "wherein at least one amino acid differs by conservative substitution from the corresponding position in SEQ ID NO:4", and the claim also recites "the amino acid sequence of which comprises amino acids from 1 to 251 of SEQ

ID NO:4" which is the narrower statement of the range/limitation. The claim cannot require both comprising amino acids 1 to 251 of SEQ ID NO:4 and differing from SEQ ID NO:4 at the same time. Either the polypeptide comprises the sequence or it differs from the sequence, but it cannot do both in the same claim.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Smallwood et al. (Proc. Natl. Acad. Sci. USA. Vol. 93, 9850-9857, 1996).

Smallwood et al. describe a number of FGF-related molecules (see abstract and Figure 1). These molecules differ by at least one conservative amino acid substitution, as required in the claim, and therefore, these molecules meet the structural limitations of the claim. The claim is anticipated by the molecules of Smallwood et al., especially in light of the limitation of "at least one" substitution, which sets no upper limit on how much of the molecule may be substituted. Since the claim fails to recite a particular activity to be retained, biological activity could be antigenicity, which would be expected to be retained in the proteins of Smallwood et al.

Applicant is again directed to the language of "at least one amino acid differs", which means that the claim encompasses differences with no upper limit and no functional limitations at all.

Conclusion

20. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The Examiner can normally be reached on Monday to Thursday from 8AM to 2PM. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §§ 1.6(d) and 1.8). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO

DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternate number. Official papers filed After Final rejection filed by fax should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud